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THE ROLE OF FOOD CONSUMPTION IN THE MORTALITY RESPONSE OF IRRADIATED RATS SUBJECTED TO PROLONGED COLD EXPOSURE

Research and Development Technical Report USNRDL-TR-172
NM 006-015
BuMed 62-03-60

21 May 1957

by

B. D. Newsom
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U.S. NAVAL RADIOLOGICAL DEFENSE LABORATORY

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Health and Biology

Technical Objective
AW-6

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ABSTRACT

In previous studies it was reported that prolonged exposure to a low ambient temperature increased the mortality rate of irradiated rats. To determine if the increased mortality is due to a failure of the irradiated rat to adapt to the higher metabolic demands of a cold environment, the food consumption of irradiated (500 and 600 r, 250-kv X rays) animals was measured during 30 days of exposure at normal (23°C) or lowered (6°C) environmental temperature. It was observed that food consumption of irradiated animals could be increased by exposure to cold; however, consumption was not sufficient to maintain body weight at a level comparable to non-irradiated animals exposed to cold.

When the food consumption of non-irradiated animals was limited by pair-feeding to that of irradiated partners during exposure to 23 and 6°C environments, the percent mortality of the pair-fed non-irradiated animals approximated the difference in mortality rates between irradiated animals maintained at 23 and 6 °C environments. These results suggest that the increased mortality rate of irradiated animals in a cold environment is related to an inadequate food intake under these conditions.

SUMMARY

The Problem

The mortality response is found to increase when animals are exposed to cold for prolonged periods following irradiation. The mechanism for this response is not known. This report is concerned with the possibility that the increase in food consumption, which is the normal response to the increased metabolic demands of a cold exposure, may not be apparent in the irradiated animal.

The Findings

Although the food consumption of irradiated rats was increased by cold exposure, the irradiated animals failed to consume sufficient food to increase their body weight at a rate comparable to that of non-irradiated animals exposed to the cold. The percent mortality of the pair-fed non-irradiated animals at 6^{o} C was comparable in magnitude to the difference in the mortality response between irradiated animals maintained at 23 and 6^{o} C environments. These findings indicate that the irradiated rat does not satisfactorily increase its caloric intake for survival at reduced ambient temperatures.

ADMINISTRATIVE INFORMATION

This work was accomplished under the Bureau of Medicine and Surgery Project Index Number NM 006-015.04, Phase 12, Technical Objective AW-6, as described in the U.S. Naval Radiological Defense Laboratory Annual Report to the Bureau of Medicine and Surgery, NavMed 1343 of 31 December 1956. This study was supported through funds provided by the School of Aviation Medicine, U.S. Air Force, and Bureau of Medicine and Surgery, U.S. Navy. Under the new plan of organization, this will be covered in the Annual Report of 31 December 1957 under Task Number 62-03-60 (Subtask 8) on DD Form 613-1.

INTRODUCTION

It is now well established that the mortality response of rats and mice to a given radiation dose is increased when these species are subjected to prolonged cold exposure following irradiation.[1,2,3] The physiological processes resulting in the altered mortality rate have not been defined. Preliminary observations made during studies of the mortality response indicated that irradiated animals subjected to a low ambient temperature consumed more food than irradiated animals maintained at normal temperatures. Despite this apparent increase in food consumption, the body weight of cold-exposed irradiated animals remained below that of the animals maintained at room temperature. The severity of the weight deficit in irradiated animals exposed to cold suggested the hypothesis that the increased mortality observed during cold exposure of irradiated rats is related to an inability to maintain sufficient caloric intake for survival at low ambient temperatures.

It was found that although the food consumption of the irradiated animal was increased upon exposure to a cold environment, consumption was not increased to the same extent as that of non-irradiated animals exposed to the same environment. In addition, the amount of food consumed by the irradiated animal was found to be inadequate for maintaining non-irradiated animals at the low environmental temperature.

GENERAL PROCEDURES

Male rats bred in this Laboratory from the Sprague-Dawley strain were used throughout the experiments. All animals were caged singly and, unless otherwise stated, were fed ad lib with Purina Laboratory chow which was pulverized sufficiently to pass through an 8-mesh screen.

The irradiation source was a 250-KVP Westinghouse X-ray unit with a .5 mm Cu + 1 mm Al filter (HVL = 1.5 mm Cu). The rats were placed in individual cells of a plastic container arranged to approximate an isodose surface and the entire chamber was rotated in the beam. The target-to-skin distance was 40 in. and the air dose was 26 r/min $\pm$ 5 percent. Twenty animals were exposed to the beam simultaneously and were distributed equally among the experimental groups for each experiment. With these procedures the midlethal dose at this Laboratory for the

Sprague-Dawley rat was approximately 580 r. All control animals were sham-irradiated.

The climatic chamber in which the animals were exposed to the low temperature environment was maintained at $6 \pm 1^{\circ}$ C and at a relative humidity of 65 ± 5 percent; the chamber volume was 512 cu ft with an air exchange of 10 cfm.

To determine the food consumption in a large sample of animals, 6-oz jars with 3-in. diameters were used as food containers. The jar was filled 3/4 full with ground food and a 3-in. iron washer with a 1-in. center hole was placed on top of the food. The washer prevented the animal from piling the food against one side of the cup and spilling it. A plastic cap having a 2-in. hole served as the container lid. The animals were able to obtain all of the food in the jar. After the animals were adapted to this feeding method for two weeks prior to the experiment, there was no food spillage. The jars were weighed daily and the food consumption computed. In an experiment designed to test the adequacy of the food-dispensing method, it was found that following irradiation with 500 r there was no difference between the rate of recovery in body weights of animals fed powdered food from these containers and animals fed with loose pellets.

In the pair-feeding experiment, the non-irradiated partner was fed an amount equivalent to the previous 24-hr consumption of the irradiated animal. If the irradiated animal died prior to its pair-fed partner, the pair-fed non-irradiated animal received an amount equivalent to the last full 24-hr food consumption of the dead animal for the next three days. If the survival time of the pair-fed animal exceeded that of the irradiated animal by 24 hr, it was considered a full 30-day survivor. The study consists of three types of experiments: (1) the food consumption and body weights of irradiated animals as a function of ambient temperature, (2) the effect of food deprivation upon symptomatology, body weight, and survival time as a function of ambient temperature, and (3) the survival rate of non-irradiated animals pair-fed to irradiated animals as a function of ambient temperature.

RESULTS AND DISCUSSION

Food Consumption and Body Weight Changes Following Irradiation as a Function of Environmental Temperature.

To determine if the irradiated animal increases its caloric intake when exposed to cold, the food consumption of irradiated and non-irradiated animals maintained at 23 and 6°C were measured daily and

body weights were determined three times a week. The experiment was performed twice, once at 500 r and again at 600 r. The effect of the cold exposure was to decrease survival rates from 93 percent at 23°C to 56 percent at 6°C for the 500 r dose and from 24 percent to 0 percent survival for the 600 r dose. All non-irradiated animals survived at both temperatures. Figure 1 summarizes the mean food consumption of the four groups during 30 days exposure to the test environments.

Following a prompt increase during the initial period of acclimatization the non-irradiated animals maintained at 6°C consumed 12 to 15 gm more food per day than those maintained at 23°C. An acute post-irradiation anorexia persisted for approximately four days in animals exposed to either dose and maintained at 23°C. The food consumption of irradiated animals in the cold environment did not decrease as much nor was the period of lowered food consumption as long as that of the irradiated animals kept at room temperature. Although the irradiated animals in the cold environment ate more food than that consumed by irradiated animals at 23°C, they did not maintain their consumption at the level of non-irradiated animals at 6°C.

The maximum weight deficit suffered by irradiated animals surviving cold exposure was approximately the same as that of irradiated animals maintained at normal room temperature (Fig. 2). Recovery from this weight loss was slower in the irradiated animals maintained at 6°C than it was in the animals maintained at 23°C. The weight curve of surviving irradiated animals in the cold environment remained below that of the irradiated animals kept at a warmer temperature throughout the period of observation. The failure of irradiated animals to gain weight in a manner comparable to non-irradiated animals in the cold environment is presumably related to the deficiency in food intake and suggests the importance of insufficient food consumption for survival in the cold following irradiation.

Effects of Food Deprivation as a Function of Environmental Temperature.

In view of the anoretic phenomenon exhibited by irradiated rats, the importance of food deprivation upon symptomatology, rate of body weight loss, and survival rate during exposure to a low environmental temperature was evaluated. Seventy male Sprague-Dawley rats were placed in individual cages and distributed into two groups. One group of 35 animals was exposed to a temperature of 6°C; the remaining group was kept at room temperature (23°C) under normal laboratory conditions. Both groups were allowed to drink water ad lib but were food-deprived.

The animals which were kept at 23°C did not appear emaciated until the tenth day of starvation; the animals maintained at 6°C however,

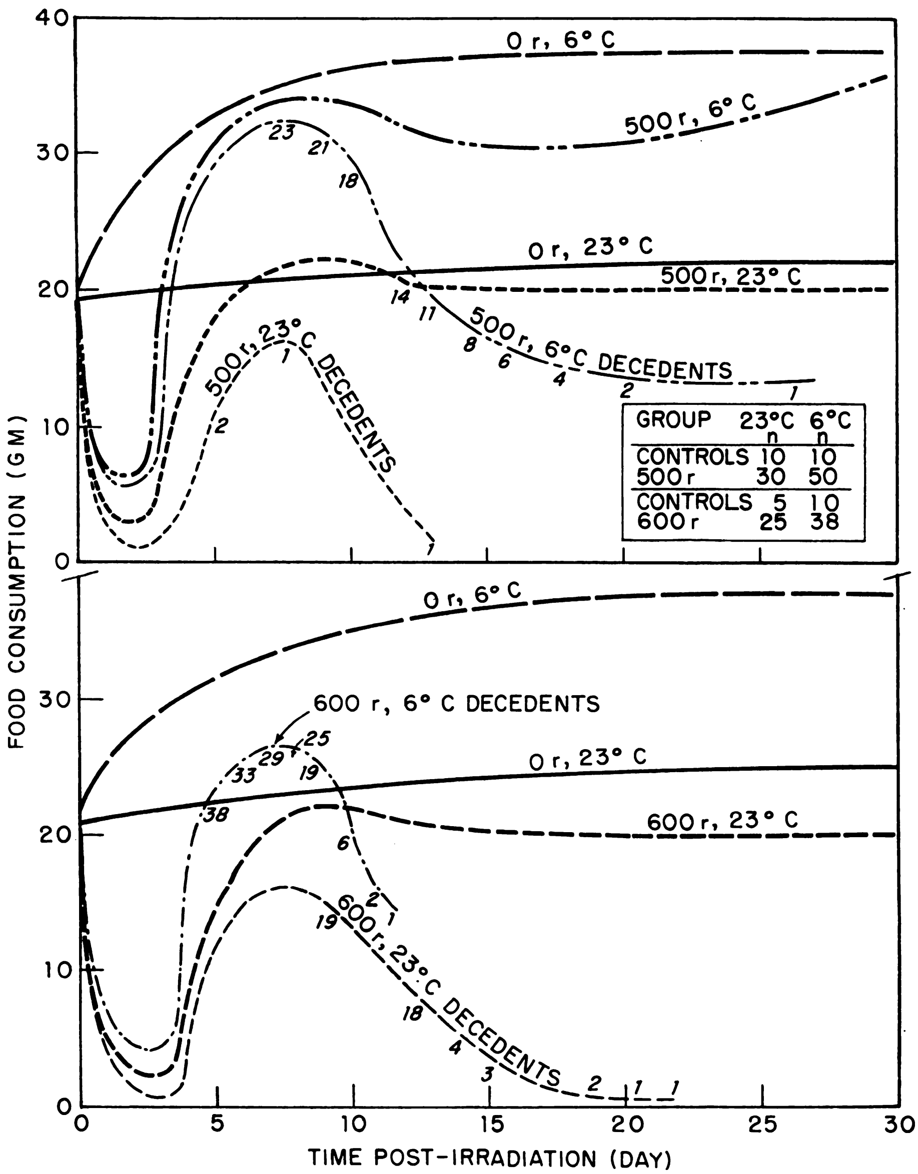

Fig. 1 Effect of Prolonged Cold Exposure on the Food Consumption of Rats Irradiated with 500 or 600 r X Rays. The number of animals remaining in the decedent groups is indicated by figures along the curves.

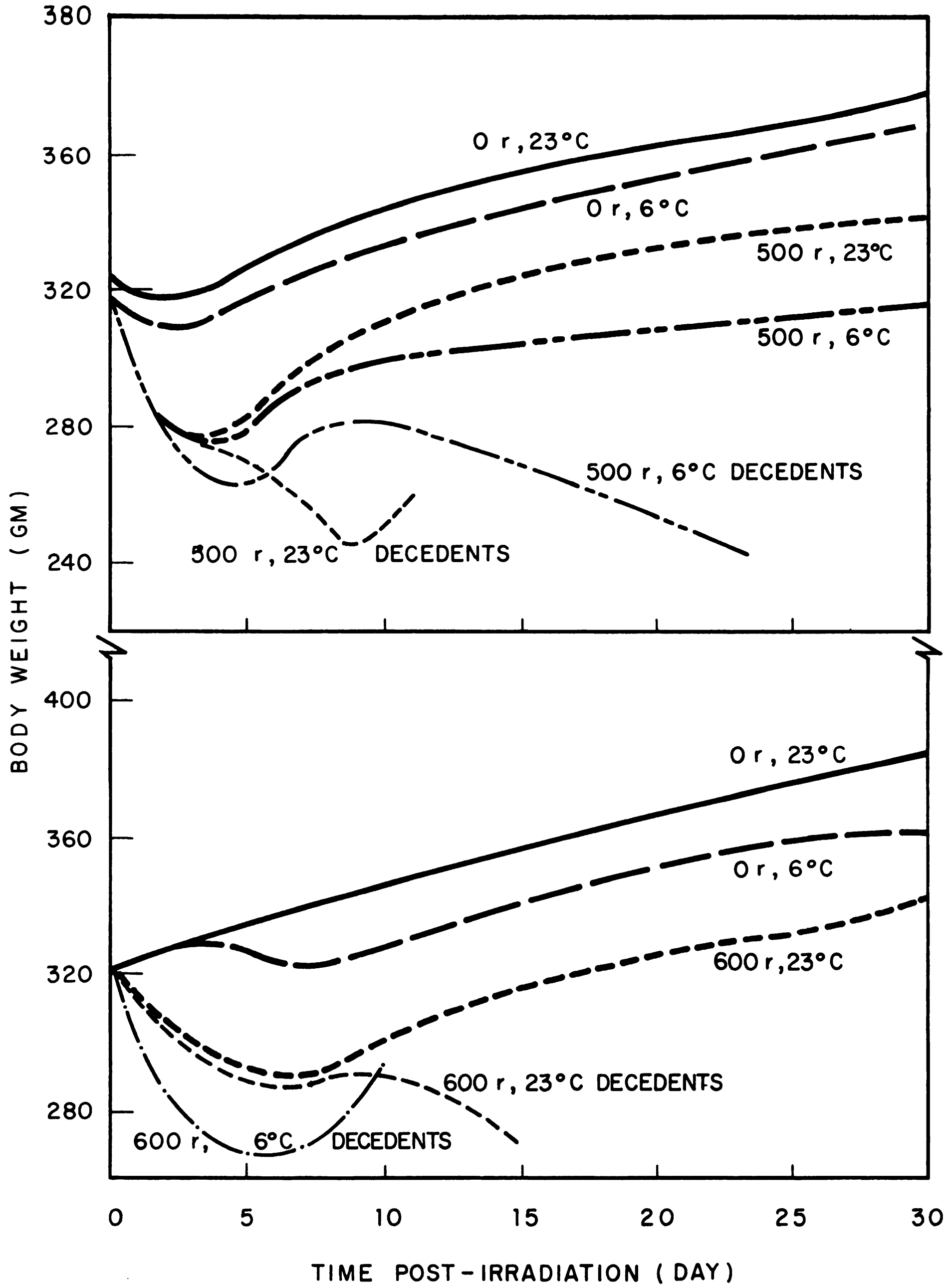

Fig. 2 Effect of Prolonged Cold Exposure on the Body Weight of Rats Irradiated with 500 or 600 r X Rays.

exhibited signs of stress after 24 hr of exposure and by the second day these animals appeared quite emaciated. The food-deprived animals kept in the cold for three days showed edema and erythema of the tails, ears, and feet; by the fifth day these animals were quite lethargic with open bleeding lesions on the feet, tails, and ears. All cold-exposed starved animals died before the first death occurred in the room-temperature starved group. Animals maintained in the cold died between the third and sixth days with a mean survival of 4.4 days. The animals starved at 23°C died between the seventh and fifteenth day with a mean survival time of 11.0 days. Figure 3 depicts the survival time and weight loss for the two food-deprived groups. In addition to these experimental groups, two groups of five animals each, one exposed to cold and one kept at normal temperature, were used as ad lib-fed controls. Both groups continually gained weight without symptoms of stress throughout the two weeks of the experiment. The extent of weight loss at death following food deprivation was dependent upon the ambient temperature. The mean weight at the time of death for animals kept at 6°C was 70.4 percent of the original weight; the mean weight of animals kept at 23°C was 57.9 percent.

Inasmuch as the symptoms of cold damage are severe during the first five days of cold exposure in food-deprived animals, it appears that the reduced food consumption observed in irradiated rats during this period may play an important role in the deleterious effects of cold exposure upon the survival.

Survival of Non-irradiated Rats Pair Fed to Irradiated Partners During Exposure to 6 or to 23°C.

If the post-irradiation decrease in food consumption is serious enough to increase the mortality rate in irradiated animals exposed to cold, it was surmised that deaths should also occur in non-irradiated animals restricted to the food intake of irradiated animals under the same environmental conditions.

To test this hypothesis, non-irradiated animals of a similar weight and age were pair-fed an amount of food equal to that consumed by irradiated animals maintained at 6 and at 23°C. The pair-fed animals were caged individually and were placed adjacent to their irradiated partners; the experiment was done twice, once at 500 r and again at 600 r. The results were similar for both radiation doses; the mortality of both the pair-fed and irradiated animals at 30 days post-irradiation is shown in Table 1. At 23°C the non-irradiated animals had a 100 percent survival when pair-fed to either 500 r animals. At 6°C, however, only 76 percent of the animals were able to survive the cold exposure when restricted

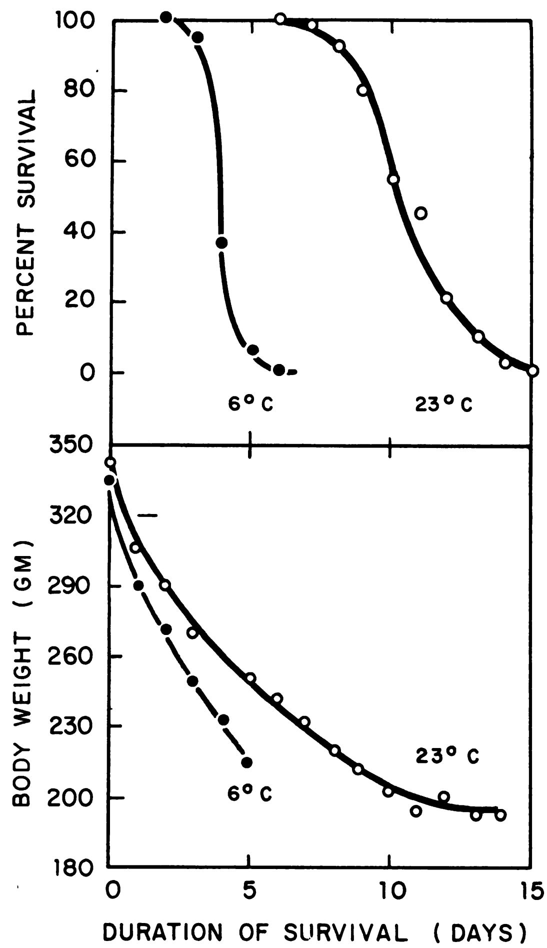

Fig. 3 Survival and Weight Loss of Food-deprived Animals at Two Ambient Temperatures. Thirty-five animals deprived at each temperature.

TABLE 1

Thirty-Day Survival of Non-Irradiated Rats Pair-Fed to Irradiated Partners at Ambient Temperatures of 6°C and 23°C

Temperature	Percent Survival Irradiation (500 r)	Pair Fed	Irradiation (600 r)	Pair Fed
23°C	93 (30)[a]	100 (30)	24 (25)	100 (25)
6°C	54 (50)	76 (50)	00 (38)	66 (38)
P	.01	.01	.01	.01

(a) Number of animals per group.

TABLE 2

The Mean Survival Time of Cold-Exposed Irradiated Decedents Classified According to the Responses of the Non-Irradiated Pair-Fed Partner

Irradiated decedents whose:	M.S.T. (days) for Irradiated Decedents (500 r)	(600 r)
Pair-fed partner survived	12.3 (12)[a]	8.5 (25)
Pair-fed partner died	17.7 (11)	10.0 (13)

(a) Number of animals.

to the amount of food consumed by partners irradiated with 500 r and only 66 percent survived when pair-fed to animals irradiated with 600 r (Table 1).

The degree of mortality produced in cold-exposed non-irradiated animals through limited food consumption is comparable in magnitude to the increase in mortality which occurs when irradiated animals are maintained at 6°C rather than 23°C. The pair-fed non-irradiated animals maintained in the cold began to show symptoms of stress after the sixth day of exposure which were similar to those observed in the starved non-irradiated animals. Erythema of the feet, tails,and ears was prevalent; in some cases this progressed to open bleeding lesions. These symptoms of cold damage were observed in the irradiated partners after the fifteenth day of exposure and were not observed in any of the *ad lib*-fed non-irradiated animals during the 30 days of exposure.

When the pair-fed partner survives and the irradiated animal dies the death must not be due to a lack of food intake, since the food consumed by the irradiated animal was sufficient to maintain the non-irradiated animal. In Table 2 it can be seen that the irradiated decedents whose pair-fed non-irradiated partners survived had a shorter mean survival time than the irradiated decedents with partners that died. This suggests that it was the later deaths, rather than the earlier ones, that were evoked by the lowered food consumption.

It is apparent that the depression in food consumption following irradiation assumes special importance for survival at a low ambient temperature. While exposure to the cold environment resulted in an increased food consumption in irradiated animals, this increase was not maintained at the level of the cold-exposed non-irradiated animals. Presumably, the inability of irradiated animals to gain weight to the extent of non-irradiated animals in the cold environment reflects, at least in part, the effect of reduced food consumption. The pair-feeding experiments indicate that when the food intake is reduced to the extent observed after irradiation under these conditions, death may ensue.

SUMMARY

A study was made to determine the role of food consumption following radiation exposure with respect to survival at a low environmental temperature. Although food consumption was increased by cold exposure, the irradiated animals failed to consume sufficient food to increase their

body weight at a rate comparable to that of non-irradiated animals in the 6°C environment during the 30-day period of observation. Approximately 30 percent of the non-irradiated animals restricted to the food intake of irradiated animals maintained at the same temperature succumbed during exposure to cold, whereas all survived at room temperature (23°C). The percent mortality of the pair-fed non-irradiated animals at 6°C was comparable in magnitude to the difference in the mortality response between irradiated animals maintained at 6°C and 23°C environments. These experiments support the hypothesis that the increased mortality response which is observed with cold exposure following irradiation in rats is related to an inability to maintain a sufficient caloric intake for survival at reduced ambient temperatures.

Approved by:

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